Journal of Bio-Molecule Research and Engineering
Vol. 2 | No. 1 |13 - 25 | 2023
e-ISSN: 2962-343X
http://www.e-journal.unair.ac.id/biome

Potential of Microbial Isolates from Indonesia in Producing Antimicrobial Compounds: A Review

Almando Geraldi[1,2*], Nabilla Hapsari Wijaya[1,2], Christopher Clement[2], and Versa Rachmania Hajar[2]

[1]University CoE-Research for Bio-Molecule Engineering, Universitas Airlangga, 60115 Surabaya, Indonesia
[2]Department of Biology, Faculty of Science and Technology, Universitas Airlangga, 60115 Surabaya, Indonesia
*Corresponding author
almando.geraldi@fst.unair.ac.id

ARTICLE INFO

Article history
Received 21st March 2023
Accepted 27th May 2023

Keywords:
antimicrobial compounds
microbial diversity
Indonesia

ABSTRACT

Indonesia, as a megabiodiverse country, possesses a wealth of beneficial microorganisms, including bacteria and fungi capable of producing antimicrobial compounds. Over the past decade, extensive research has been conducted in Indonesia to explore and screen the antimicrobial activities of bacteria and fungi. These microorganisms have been isolated from various ecosystems, such as terrestrial, maritime, extreme environments like hot springs and sand dunes, as well as from animals and plants hosts. Most studies have focused on the antimicrobial activity of crude metabolite extracts, which demonstrate inhibitory effects against clinically significant pathogens, including Methicillin-resistant *Staphylococcus aureus*, multidrug-resistant *Escherichia coli*, and *Salmonella typhi*. This review systematically synthesizes findings from peer-reviewed literature, detailing isolation strategies, antimicrobial screening techniques, and the bioactivities reported. By consolidating current knowledge, it aims to elucidate the potential of Indonesia's microbial resources for developing novel antimicrobial agents and promoting their sustainable exploitation within the context of global health challenges.

1. Introduction

The misuse of antibiotics has precipitated the emergence of antibiotic resistance, an alarming global health crisis [1], [2]. The proliferation of antibiotic-resistant microbial strains presents a grave threat to worldwide healthcare systems, with the potential to instigate pandemics. Several antibiotic-resistant strains, such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), multi-drug-resistant *Escherichia coli*, and multidrug-resistant tuberculosis, have already surfaced [3]. As a result, extensive research endeavors are underway to explore antimicrobial compounds from diverse sources, encompassing plants, animals, as well as microorganisms like bacteria and fungi.

Exploration of organisms yielding antimicrobial compounds is a global undertaking. Plants, for instance, harbor secondary metabolites like flavonoids, quinones, and alkaloids, which disrupt the cell walls and membranes, and hinder protein synthesis and nucleic acid processes in pathogenic microbes [4], [5], [6]. Essential oils from *Cinnamomum verum*, *Eucalyptus globulus*, and *Syzygium* *aromaticum* have been reported to inhibit MRSA growth [7]. Clove extract (*Syzygium aromaticum*) is documented to exhibit inhibitory activity against antibiotic-resistant Gram-negative bacteria [8]. Plant extracts from the Zingiberaceae family are known to possess antifungal activity against *Candida albicans* [9]. Conversely, antimicrobial compounds produced by animals primarily include antimicrobial peptides (AMP) that disrupt cell membranes and interact with macromolecules within cells [10], [11]. AMPs produced by the frog *Limnonectes fujianensis* have been reported to inhibit MRSA growth, while AMPs from the Horseshoe Crab (*Tachypleus tridentatus*) demonstrate antimicrobial activity against MRSA and Extended-spectrum-β-Lactamase (ESBL)-producing *E. coli* [12], [13].

Microorganisms, such as bacteria and fungi, have proven to be a rich source of antimicrobial compounds, many of which have been commercialized, including penicillin, streptomycin, and actinomycin [14], [15]. Moreover, they also produce a range of other antimicrobial compounds, such as pigments, alkylphenols, terpenoids, and nonribosomal peptides [16], [17].

Microorganisms offer the advantage of rapid growth and minimal space requirements for antimicrobial compound production. Bacteria and fungi can produce these compounds within days or weeks. In contrast, plant tissue and animal cell cultures for antimicrobial compound production require more time, involve intricate procedures, and incur higher costs. Additionally, the space needed for production is relatively minimal, often confined to a few square meters, owing to the ability to perform production processes in fermentors, unlike medicinal plants, that require extensive land for cultivation.

Indonesia, known as one of the biodiversity hotspots, has conducted extensive exploration of microorganisms producing antimicrobial compounds [18], [19]. Yet, there is currently a lack of scientific literature summarizing research on microorganisms yielding antimicrobial compounds in Indonesia. Such a comprehensive review would be crucial for formulating strategies to develop antimicrobial therapeutics. This review aims to encompass various bacteria and fungi from Indonesia that produce antimicrobial compounds, and summarize the progress in exploring these microorganisms and outlining potential avenues for future research.

2. Exploration of Antimicrobes-producing bacteria in Indonesia

In the past decade, extensive exploration of bacteria producing antimicrobial compounds has been carried out across various Indonesian ecosystems. As shown in Table 1, bacteria with antimicrobial activity have been successfully isolated from marine ecosystems, such as mangroves and tidal mudflats, extreme environments like hot springs and sand dunes, and fermented foods. Some microbes are associated with animals as endosymbionts or with plants as endophytic bacteria. Most of the bacteria producing antimicrobial compounds that have been isolated belong to the genera *Bacillus*, *Streptomyces*, and *Lactobacillus*, known for their antimicrobial compound production.

Table 1. Bacteria producing antimicrobial compounds isolated from Indonesia

Sources	Bacteria species	Antimicrobial activity	Reference
Green cacao fermentation process in West Sumatra	*L. brevis*	Culture free supernatant showed growth inhibition towards pathogenic *E. coli*	[20]
Marine sea slugs from North Sulawesi	*M. communis, Pseudoalteromonas* sp., *Vibrio* sp.	Ethyl acetate extract of the bacterial culture showed moderate to strong growth inhibition towards Methicillin-Resistant *Staphylococcus aureus* or Enterohaemorrhagic *E. coli*.	[21]
Rhizospheric soil of mangrove forests in Gorontalo	*Streptomyces* sp.	Acetone extracts of the bacterial culture showed bacteriostatic activity towards *E. coli*, *S. aureus*, and *Bacillus subtilis* with Minimum Inhibitory Concentration (MIC) value of 0.094, 0.125 and 0.280 mgmL-1, respectively. Acetone and ethyl acetate extracts of the bacterial culture showed fungistatic activity towards *Aspergillus niger* and *Candida albicans* with Minimum Inhibitory Concentration (MIC) value of 0.125 and 0.250 mgmL-1, respectively.	[22]

Seagrasses from North Java Sea	*B. flexus*, *Streptomyces lienomycini*	Ethyl acetate extract of the bacterial culture showed growth inhibition towards Methicillin-Resistant *Staphylococcus aureus* and Multidrugs resistant *E. coli*	[23]
Intestines from domestic chicken (*Gallus domesticus*) from South Sulawesi	*B. subtilis* strain PATA-5.	Bacterial culture showed inhibition towards *E. coli*	[24]
Peat soil from South Kalimantan	Bacteria from family Enterobacteriaceae and Bacillaceae	Culture free supernatant showed growth inhibition towards Extended-spectrum β-lactamases-producing *E. coli* and Methicillin-Resistant *Staphylococcus aureus*	[25]
Coral reef ecosystems of Alor Island	*Pseudoalteromonas rubra*	Prodiginine pigments produced by *P. rubra* showed growth inhibition towards pathogenic bacteria *E. coli*, *S. aureus*, *Salmonella typhi*, and yeast *C. albicans*	[26]
Traditional fermented milk (dadih) from West Sumatra	*L. plantarum*	Culture free supernatant showed growth inhibition towards *E. coli* O157.	[27]

Rhizosperic soil in Pramuka Island, Jakarta	*Streptomyces badius*	Ethyl acetate extracts of the bacterial culture showed bacteriostatic activity towards *E. coli, S. aureus,* and *B. subtilis* with Minimum Inhibitory Concentration (MIC) value of 3.125, 6. 25 and 31.25 μgmL-1, respectively.	[28]
Mangrove soil in Tuban, East Java	*Streptomyces vellosus*	Culture free supernatant showed growth inhibition towards *E. coli* ATCC 25922.	[29]
Coastal sand dunes in Yogyakarta	*B. megaterium, B. velezensis*	• Culture free supernatant of *B. megaterium* showed growth inhibition towards *E. coli* and *P. aeruginosa*. • Culture free supernatant of *B. megaterium* showed growth inhibition towards *E. coli* and *P. aeruginosa*.	[30]
Hot springs in North Sumatra	*B. megaterium*	Culture free supernatant showed growth inhibition towards *E. coli* and *S. aureus*.	[31]

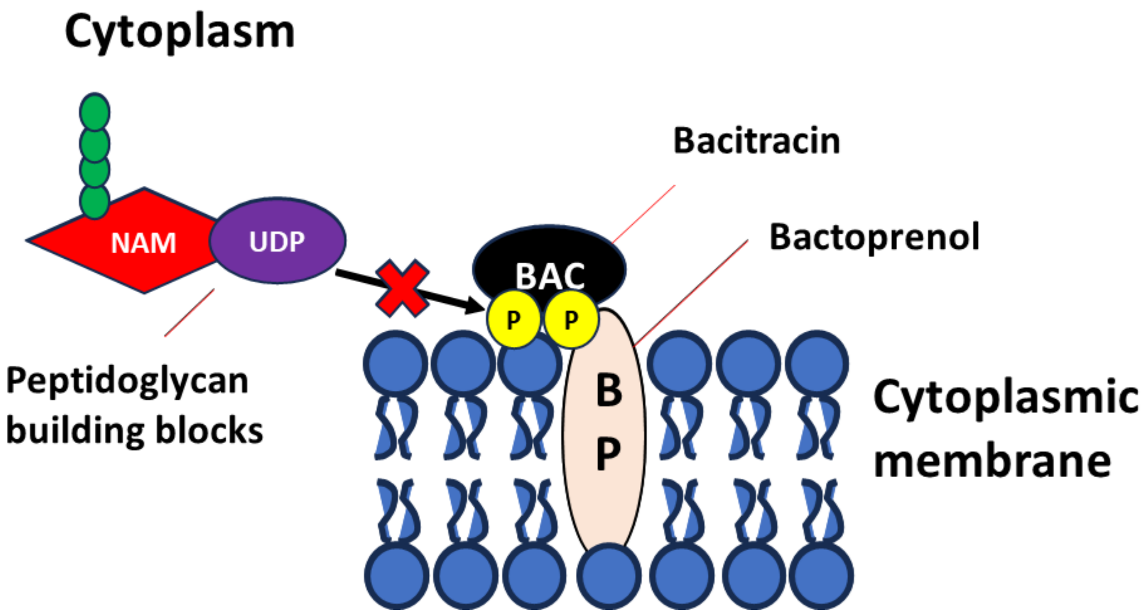

Figure 1. Illustration of the antibacterial mechanism of bacitracin by inhibiting the transport of peptidoglycan building blocks.

Bacteria from the genus *Bacillus*, known for their ability to produce antimicrobial compounds, have been isolated from various sources in Indonesia, including peat soil, seaweed (as endophytic bacteria), and extreme ecosystems like sand dunes and hot springs. *Bacillus* is a cosmopolitan genus, making it adaptable to various ecosystems [32], [33]. *Bacillus* sp. can produce antimicrobial compounds for survival, including bacitracin, which disrupts cell wall integrity (Figure 1), aurantinin, causing plasma membrane lysis, and zwittermicin A, inhibiting transcription and DNA replication [34], [35], [36].

Streptomyces, the largest genus in the phylum Actinobacteria, is renowned for producing antibiotics [37]. As indicated in Table 1, *Streptomyces* has been isolated from various terrestrial and aquatic ecosystems in Indonesia [38]. Some commercially important antibiotics produced by Streptomyces include streptomycin, daptomycin, chloramphenicol, tetracycline, and kanamycin [39]. Additionally, *Lactobacillus*, commonly used as probiotics, is known to produce antimicrobial compounds such as lantibiotics and bacteriocins [40].

Notably, interesting findings in Indonesian research include the antimicrobial activities of bacteria species such as *Marinomonas communis* and *Pseudoalteromonas rubra*. The genus *Marinomonas* was previously reported to produce antimicrobial proteins like lysine oxidase and marinocine [41], [42]. In Table 1, it can be observed that the prodiginine pigment from *P. rubra* is the only pure compound extracted and found to exhibit antimicrobial activity [21]. Apart from prodiginine pigment, *P. rubra* has also been reported to produce the antimicrobial compound isatin [43].

3. Exploration of Antimicrobial compounds-producing fungi in Indonesia

Fungi are known to produce a wide range of antimicrobial compounds, including antibiotics. As shown in Table 2, over the past decade, most fungal isolates with antimicrobial activity in Indonesia have been associated with both terrestrial and marine animals and plants, with dominant genera being *Aspergillus* and *Trichoderma*. Similar to bacteria, crude metabolite extracts from fungi have been used in antimicrobial activity tests in the most of the studies presented in Table 2.

Table 2. Fungi producing antimicrobial compounds isolated from Indonesia

Sources	Fungi species	Antimicrobial activity	Reference
Artemisian annua plant from Tawangmangu, Central Java	E2 species	Ethyl acetate extracts of the mycelium free supernatant of E2 showed growth inhibition towards *B. subtilis, E. coli,* and *S. typhi.*	[44]
Marine sponge from Jepara, Central Java	*Trichoderma parareesei*	Fungal pigment extracted using methanol showed inhibition towards *E. coli and S. typhi.*	[45]
Mangrove plant (*Sonneratia griffithii*) from West Sumatra	*Aspergillus niger*, *Candida* sp.	Butanol and Ethyl acetate extracts of the fungal liquid culture showed growth inhibition towards *S. aureus* and *E. coli*.	[46]
Marine sponge (*Stylissa flabelliformis*) from Menjangan Island, Bali	*Trichoderma reesei*	Methanol extracts of the fungal culture showed growth inhibition towards *E. coli*, Methicillin Resistant *S. aureus*, and *C. albicans*.	[47]
Macroalgae (*Euchema* sp.)	*Aspergillus elegans*	Ethyl acetate extracts and isolated antimicrobial compound of the mycelium free supernatant of *A. elegans* showed growth inhibition	[48]

		towards *B. subtilis, E. coli and S. aureus.*	
Marine sponge (Stylissa flabelliformis) from Karimunjawa National Park, Central Java	*Aspergillus nomius*	*Aspergillus nomius* showed growth inhibition towards multi drug resistant *Acinetobacter baumannii*	[49]
Leaves of *Coleus ambonicus*	*Athelia rolfsii*	Ethyl acetate extracts of the mycelium free supernatant of *A. rolfsii* showed growth inhibition towards *B. subtilis, E. coli,* and *S. aureus*.	[50]
Marine Sponge *Chelonaplysilla* sp from Mandeh Island, West Sumatra	*Aspergillus mellinus, Phomapsis* sp.	Ethyl acetate extracts of the fungal culture showed growth inhibition towards *S. aureus*, and *E. coli*.	[51]
Mangrove plant (*Sonneratia alba*) from Timor Island	*Aspergillus flavus*	Kojic acid produced by A. flavus showed growth inhibition towards *S. aureus*, and *E. coli*.	[52]
Medicinal plant (*Lannea coromandelica*) from South Sulawesi	*Penicillium* sp.	Ethyl acetate extracts of the mycelium free supernatant of *A. rolfsii* showed growth inhibition towards *S. typhi* and *S. aureus*.	[53]

Indomalayan termite (*Macrotermes gilvus* Hagen) mound from Bogor, West Java	*Fungus combs* (probably mix species)	● Ethyl acetate extract from fungus combs exhibited high antimicrobial activity against *S. aureus*, *E. coli*, *P. aeruginosa*, *A. flavus*, and *A. niger*. ● Ethyl acetate extract of the fungus mound has Minimum Inhibitory Concentration and Minimum Fungicidal Concentration towards tested *Aspergillus* species of 0.78 and 1.56 mgmL-1, respectively.	[54]
Sea squirt (*Eudistoma* sp) from Bunaken Island, North Sulawesi	*Trichoderma asperellum*	Ethyl acetate extracts of the fungal culture showed growth inhibition towards *C. albicans*, *Aeromonas hydrophila*, *Salmonella* sp., *S. aureus*, and *E. coli*.	[55]

The genus *Aspergillus* is known to produce antimicrobial compounds such as aspergillin, fumagillin, secofumitremorgins, sphingofungin, and kojic acid [5], [56], [57]. Meanwhile, *Trichoderma*, commonly used as a biocontrol agent in agriculture, has also been reported to produce compounds that inhibit human pathogenic bacteria [58], [59]. An intriguing discovery is the antimicrobial activity of *Athelia rolfsii*, previously known as a phytopathogenic fungus [60].

4. Conclusions

In the past decade, extensive exploration of bacteria and fungi producing antimicrobial compounds has been conducted across various ecosystems in Indonesia. In most studies, crude metabolite extracts from these microorganisms have exhibited antimicrobial activity. In the future, there is a need to isolate pure compounds and formulate them for the development of antimicrobial drugs based on these compounds.

References

[1] M. M. Aljeldah, "Antimicrobial Resistance and Its Spread Is a Global Threat," *Antibiotics*, vol. 11, no. 8, 2022, doi: 10.3390/antibiotics11081082.

[2] S. Yadav and A. Kapley, "Antibiotic resistance: Global health crisis and metagenomics," *Biotechnology Reports*, vol. 29, p. e00604, 2021, doi: 10.1016/j.btre.2021.e00604.

[3] V. P. Alonso, M. M. Queiroz, M. L. Gualberto, and M. S. Nascimento, "Klebsiella pneumonia carbapenemase (KPC), methicillin-resistant Staphylococcus aureus (MRSA), and vancomycin-resistant Enterococcus spp. (VRE)in the food production chain and biofilm formation on abiotic surfaces," *Current Opinion in Food Science*, vol. 26, pp. 79–86, 2019, doi: 10.1016/j.cofs.2019.04.002.

[4] Y. Xie, J. Chen, A. Xiao, and L. Liu, "Antibacterial activity of polyphenols: Structure-activity relationship and influence of hyperglycemic condition," *Molecules*, vol. 22, no. 11, 2017, doi: 10.3390/molecules22111913.

[5] L. H. Yan, X. M. Li, L. P. Chi, X. Li, and B. G. Wang, "Six new antimicrobial metabolites from the deep-sea sediment-derived fungus aspergillus fumigatus SD-406," *Marine Drugs*, vol. 20, no. 1, pp. 1–14, 2022, doi: 10.3390/md20010004.

[6] N. Vaou, E. Stavropoulou, C. Voidarou, C. Tsigalou, and E. Bezirtzoglou, "Towards advances in medicinal plant antimicrobial activity: A review study on challenges and future perspectives," *Microorganisms*, vol. 9, no. 10, pp. 1–28, 2021, doi: 10.3390/microorganisms9102041.

[7] T. Ali *et al.*, "Antibacterial activity of plant essential oils against indigenously characterized methicillin-resistant Staphylococcus aureus (MRSA)," *Tropical Biomedicine*, vol. 39, no. 1, pp. 17–25, 2022, doi: 10.47665/tb.39.1.005.

[8] S. S. Faujdar, D. Bisht, and A. Sharma, "Antibacterial activity of Syzygium aromaticum (clove) against uropathogens producing ESBL, MBL, and AmpC beta-lactamase: Are we close to getting a new antibacterial agent?," *Journal of Family Medicine and Primary Care*, vol. 9, no. 1, pp. 180–186, 2020, doi: 10.4103/jfmpc.jfmpc.

[9] A. Geraldi *et al.*, "Tropical Medicinal Plant Extracts from Indonesia as Antifungal Agents against Candida Albicans," *Frontiers in Bioscience - Landmark*, vol. 27, no. 9, Sep. 2022, doi: 10.31083/j.fbl2709274.

[10] A. H. Benfield and S. T. Henriques, "Mode-of-Action of Antimicrobial Peptides: Membrane Disruption vs. Intracellular Mechanisms," *Frontiers in Medical Technology*, vol. 2, no. December, pp. 25–28, 2020, doi: 10.3389/fmedt.2020.610997.

[11] B. P. Lazzaro, M. Zasloff, and J. Rolff, "Antimicrobial peptides: Application informed by evolution," *Science*, vol. 368, no. 6490, 2020, doi: 10.1126/science.aau5480.

[12] Y. Yuan *et al.*, "A novel membrane-disruptive antimicrobial peptide from frog skin secretion against cystic fibrosis isolates and evaluation of anti-MRSA effect using Galleria mellonella model," *Biochimica et Biophysica Acta - General Subjects*, vol. 1863, no. 5, pp. 849–856, 2019, doi: 10.1016/j.bbagen.2019.02.013.

[13] W. F. Wang *et al.*, "Identification of a Novel Antimicrobial Peptide From the Ancient Marine Arthropod Chinese Horseshoe Crab, Tachypleus tridentatus," *Frontiers in Immunology*, vol. 13, no. March, pp. 1–15, 2022, doi: 10.3389/fimmu.2022.794779.

[14] G. A. Durand, D. Raoult, and G. Dubourg, "International Journal of Antimicrobial Agents Antibiotic discovery : history , methods and perspectives," vol. 53, pp. 371–382, 2019.

[15] M. Hutchings, A. Truman, and B. Wilkinson, "Antibiotics: past, present and future," *Current Opinion in Microbiology*, vol. 51, no. Figure 1, pp. 72–80, 2019, doi: 10.1016/j.mib.2019.10.008.

[16] R. Srinivasan, A. Kannappan, C. Shi, and X. Lin, "Marine bacterial secondary metabolites: A treasure house for structurally unique and effective antimicrobial compounds," *Marine Drugs*, vol. 19, no. 10, pp. 1–36, 2021, doi: 10.3390/md19100530.

[17] C. K. Venil, L. Dufossé, and P. Renuka Devi, "Bacterial Pigments: Sustainable Compounds With Market Potential for Pharma and Food Industry," *Frontiers in Sustainable Food Systems*, vol. 4, no. July, pp. 1–17, 2020, doi: 10.3389/fsufs.2020.00100.

[18] I. Sanka *et al.*, "Synthetic biology in Indonesia: Potential and projection in a country with mega biodiversity," *Biotechnology Notes*, vol. 4, no. December 2022, pp. 41–48, 2023, doi: 10.1016/j.biotno.2023.02.002.

[19] H. Y. S. H. Nugroho *et al.*, "Mainstreaming Ecosystem Services from Indonesia's Remaining Forests," *Sustainability (Switzerland)*, vol. 14, no. 19, 2022, doi: 10.3390/su141912124.

[20] S. Syukur, "Antimicrobial Properties and Lactase Activities from Selected Probiotic Lactobacillus brevis Associated With Green Cacao Fermentation in West Sumatra, Indonesia," *Journal of Probiotics & Health*, vol. 01, no. 04, pp. 4–7, 2013, doi: 10.4172/2329-8901.1000113.

[21] N. Böhringer *et al.*, "Antimicrobial potential of bacteria associated with marine sea slugs from North Sulawesi, Indonesia," *Frontiers in Microbiology*, vol. 8, no. JUN, pp. 1–8, 2017, doi: 10.3389/fmicb.2017.01092.

[22] Y. Retnowati, S. Moeljopawiro, T. S. Djohan, and E. S. Soetarto, "Antimicrobial activities of actinomycete isolates from rhizospheric soils in different mangrove forests of Torosiaje, Gorontalo, Indonesia," *Biodiversitas*, vol. 19, no. 6, pp. 2196–2203, 2018, doi: 10.13057/biodiv/d190627.

[23] O. Cristianawati *et al.*, "Screening of antibacterial activity of seagrass-associated bacteria from the North Java Sea, Indonesia against multidrug-resistant bacteria," *AACL Bioflux*, vol. 12, no. 4, pp. 1054–1064, 2019.

[24] D. R. Husain, S. Gunawan, and S. Sulfahri, "Antimicrobial potential of lactic acid bacteria from domestic chickens (Gallus domesticus) from south celebes, indonesia, in different growth phases: In vitro experiments supported by computational docking," *Iranian Journal of Microbiology*, vol. 12, no. 1, pp. 62–69, 2020, doi: 10.18502/ijm.v12i1.2519.

[25] D. Mahdiyah *et al.*, "Screening of Indonesian peat soil bacteria producing antimicrobial compounds," *Saudi Journal of Biological Sciences*, vol. 27, no. 10, pp. 2604–2611, 2020, doi: 10.1016/j.sjbs.2020.05.033.

[26] E. Setiyono, M. A. S. Adhiwibawa, R. Indrawati, M. N. U. Prihastyanti, Y. Shioi, and T. H. P. Brotosudarmo, "An Indonesian Marine Bacterium, Pseudoalteromonas rubra, Produces Antimicrobial Prodiginine Pigments," *ACS Omega*, vol. 5, no. 9, pp. 4626–4635, 2020, doi: 10.1021/acsomega.9b04322.

[27] H. Harun, Y. Wirasti, B. Purwanto, and E. Purwati, "Characterization of lactic acid bacteria and determination of antimicrobial activity in dadih from air dingin alahan panjang district, solok regency-west sumatera," *Systematic Reviews in Pharmacy*, vol. 11, no. 3, pp. 583–586, 2020, doi: 10.31838/srp.2020.3.76.

[28] S. Setiawati *et al.*, "The potency of actinomycetes extracts isolated from pramuka island, jakarta, indonesia as antimicrobial agents," *Biodiversitas*, vol. 22, no. 3, pp. 1104–1111, 2021, doi: 10.13057/biodiv/d220304.

[29] Fatimah *et al.*, "Antimicrobial activity of actinomycetes isolated from mangrove soil in Tuban, Indonesia," *Biodiversitas*, vol. 23, no. 6, pp. 2957–2965, 2022, doi: 10.13057/biodiv/d230622.

[30] A. Geraldi *et al.*, "Screening of antibacterial activities of Bacillus spp. isolated from the Parangkusumo coastal sand dunes, Indonesia," *BIO Integration*, vol. 3, no. 3, pp. 132–137, 2022, doi: 10.15212/bioi-2022-0005.

[31] C. N. Ginting, F. Piska, Harmileni, and E. Fachrial, "Molecular identification of thermophilic bacteria with antimicrobial activity isolated from hot springs in North Sumatra, Indonesia," *Biodiversitas*, vol. 24, no. 2, pp. 752–758, 2023, doi: 10.13057/biodiv/d240210.

[32] S. Polonca, "Environment Shapes the Intra-species Diversity of Bacillus subtilis Isolates," *Microbial Ecology*, vol. 79, no. 4, pp. 853–864, 2020, doi: 10.1007/s00248-019-01455-y.

[33] B. K. Kashyap, M. K. Solanki, and A. K. Pandey, “Plant Health Under Biotic Stress,” *Plant Health Under Biotic Stress*, pp. 219–236, 2019, doi: 10.1007/978-981-13-6040-4.

[34] C. Tran, I. E. Cock, X. Chen, and Y. Feng, “Antimicrobial Bacillus: Metabolites and Their Mode of Action,” *Antibiotics*, vol. 11, no. 1, 2022, doi: 10.3390/antibiotics11010088.

[35] M. Fazle Rabbee and K. H. Baek, “Antimicrobial Activities of Lipopeptides and Polyketides of Bacillus velezensis for Agricultural Applications,” *Molecules (Basel, Switzerland)*, vol. 25, no. 21, 2020, doi: 10.3390/molecules25214973.

[36] S. Caulier, C. Nannan, A. Gillis, F. Licciardi, C. Bragard, and J. Mahillon, “Overview of the antimicrobial compounds produced by members of the Bacillus subtilis group,” *Frontiers in Microbiology*, vol. 10, no. FEB, pp. 1–19, 2019, doi: 10.3389/fmicb.2019.00302.

[37] G. A. Quinn, A. M. Banat, A. M. Abdelhameed, and I. M. Banat, “Streptomyces from traditional medicine: sources of new innovations in antibiotic discovery,” *Journal of Medical Microbiology*, vol. 69, no. 8, pp. 1040–1048, 2020, doi: 10.1099/jmm.0.001232.

[38] L. Donald, A. Pipite, R. Subramani, J. Owen, R. A. Keyzers, and T. Taufa, “Streptomyces: Still the Biggest Producer of New Natural Secondary Metabolites, a Current Perspective,” *Microbiology Research*, vol. 13, no. 3, pp. 418–465, 2022, doi: 10.3390/microbiolres13030031.

[39] K. Alam *et al.*, “Streptomyces: The biofactory of secondary metabolites,” *Frontiers in Microbiology*, vol. 13, no. September, pp. 1–21, 2022, doi: 10.3389/fmicb.2022.968053.

[40] M. P. Mokoena, C. A. Omatola, and A. O. Olaniran, “Applications of lactic acid bacteria and their bacteriocins against food spoilage microorganisms and foodborne pathogens,” *Molecules*, vol. 26, no. 22, 2021, doi: 10.3390/molecules26227055.

[41] P. Lucas-Elío, D. Gómez, F. Solano, and A. Sanchez-Amat, “The antimicrobial activity of marinocine, synthesized by Marinomonas mediterranea, is due to hydrogen peroxide generated by its lysine oxidase activity,” *Journal of Bacteriology*, vol. 188, no. 7, pp. 2493–2501, 2006, doi: 10.1128/JB.188.7.2493-2501.2006.

[42] D. Gómez, P. Lucas-Elío, F. Solano, and A. Sanchez-Amat, “Both genes in the Marinomonas mediterranea lodAB operon are required for the expression of the antimicrobial protein lysine oxidase,” *Molecular Microbiology*, vol. 75, no. 2, pp. 462–473, 2010, doi: 10.1111/j.1365-2958.2009.07000.x.

[43] D. Ayuningrum *et al.*, “Tunicate-associated bacteria show a great potential for the discovery of antimicrobial compounds,” *PLoS ONE*, vol. 14, no. 3, pp. 1–14, 2019, doi: 10.1371/journal.pone.0213797.

[44] P. Astuti, W. Wahyono, T. Nuryastuti, I. Purwantini, and P. Purwanto, “Antimicrobial and Cytotoxic Activities of Endophytic Fungi Isolated from Artemisia annua L,” *Journal of Applied Pharmaceutical Science*, vol. 4, no. 10, pp. 47–50, 2014, doi: 10.7324/japs.2014.401009.

[45] M. T. Sibero, D. W. Triningsih, O. K. Radjasa, A. Sabdono, and A. Trianto, “Evaluation of Antimicrobial Activity and Identification of Yellow Pigmented Marine Sponge-Associated Fungi from Teluk Awur, Jepara, Central Java,” *Indonesian Journal of Biotechnology*, vol. 21, no. 1, p. 1, 2017, doi: 10.22146/ijbiotech.26058.

[46] D. Handayani, H. Rivai, M. Hutabarat, and R. Rasyid, “Antibacterial activity of endophytic fungi isolated from mangrove plant Sonneratia griffithii Kurz,” *Journal of Applied Pharmaceutical Science*, vol. 7, no. 4, pp. 209–212, 2017, doi: 10.7324/JAPS.2017.70431.

[47] E. P. Setyowati, S. U. T. Pratiwi, Purwantiningsih, and P. O. Samirana, “Antimicrobial activity and Identification of fungus associated Stylissa flabelliformis sponge collected from Menjangan Island West Bali National Park, Indonesia,” *Indonesian Journal of Pharmacy*, vol. 29, no. 2, pp. 66–73, 2018, doi: 10.14499/indonesianjpharm29iss2pp66.

[48] H. Mulyani, R. T. Dewi, and Chaidir, “Antibacterial Compound from Aspergillus elegans SweF9 an Endophytic Fungus from Macroalgae Euchema sp.,” *Indonesian Journal of Pharmacy*, vol. 30, no. 3, pp. 217–224, 2019, doi: 10.14499/indonesianjpharm30iss3pp217.

[49] A. Sabdaningsih *et al.*, “Anti MDR acinetobacter baumannii of the sponges-associated fungi from Karimunjawa national park,” *AACL Bioflux*, vol. 12, no. 5, pp. 1970–1983, 2019.

[50] P. Astuti, R. Rollando, S. Wahyuono, and A. Nurrochmad, “Antimicrobial activities of isoprene compounds produced by an endophytic fungus isolated from the leaves of Coleus amboinicus Lour,” *Journal of Pharmacy and Pharmacognosy Research*, vol. 8, no. 4, pp. 280–289, 2020.

[51] D. Handayani, M. A. Artasasta, N. Safirna, D. F. Ayuni, T. E. Tallei, and T. Hertiani, “Fungal isolates from marine sponge Chelonaplysilla sp.: Diversity, antimicrobial and cytotoxic activities,” *Biodiversitas*, vol. 21, no. 5, pp. 1954–1960, 2020, doi: 10.13057/biodiv/d210523.

[52] A. R. B. Ola, C. A. P. Soa, Y. Sugi, T. Da Cunha, H. L. L. Belli, and H. J. D. Lalel, “Antimicrobial metabolite from the endophytic fungi aspergillus flavus isolated from sonneratia Alba, a mangrove plant of Timor-Indonesia,” *Rasayan Journal of Chemistry*, vol. 13, no. 1, pp. 377–381, 2020, doi: 10.31788/RJC.2020.1315585.

[53] P. Amelia, P. A. K. Ivada, N. Fitriana, I. Komala, S. Bahri, and and M. Hanafi, “Antioxidant And Antimicrobial Activity Of Secondary Metabolite Produced By Endophytic Fungi Isolated From Lannea Coromandelica (Houtt.) Merr,” vol. 12, no. 3, pp. 1588–1592, 2021, doi: 10.13040/IJPSR.0975-8232.12(3).1588-92.

[54] L. D. Witasari *et al.*, “Antimicrobial activities of fungus comb extracts isolated from Indomalayan termite (Macrotermes gilvus Hagen) mound,” *AMB Express*, vol. 12, no. 1, 2022, doi: 10.1186/s13568-022-01359-0.

[55] D. A. Sumilat, R. A. J. Lintang, S. L. Undap, A. A. Adam, and T. E. Tallei, “Phytochemical, antioxidant, and antimicrobial analysis of Trichoderma asperellum isolated from ascidian Eudistoma sp,” *Journal of Applied Pharmaceutical Science*, vol. 12, no. 4, pp. 90–95, 2022, doi: 10.7324/JAPS.2022.120410.

[56] F. S. Youssef, E. Alshammari, and M. L. Ashour, “Bioactive alkaloids from genus aspergillus: Mechanistic interpretation of their antimicrobial and potential sars-cov-2 inhibitory activity using molecular modelling,” *International Journal of Molecular Sciences*, vol. 22, no. 4, pp. 1–22, 2021, doi: 10.3390/ijms22041866.

[57] A. A. Al-Fakih and W. Q. A. Almaqtri, “Overview on antibacterial metabolites from terrestrial Aspergillus spp,” *Mycology*, vol. 10, no. 4, pp. 191–209, 2019, doi: 10.1080/21501203.2019.1604576.

[58] M. Sood, D. Kapoor, V. Kumar, and M. S. Sheteiwy, “Trichoderma : The ‘ Secrets ’ of a Multitalented,” *Plants*, vol. 9, p. 762, 2020.

[59] F. V. Ferreira and M. A. Musumeci, “Trichoderma as biological control agent: scope and prospects to improve efficacy,” *World Journal of Microbiology and Biotechnology*, vol. 37, no. 5, pp. 1–17, 2021, doi: 10.1007/s11274-021-03058-7.

[60] G. K. Patra, G. K. Acharya, J. Panigrahi, A. K. Mukherjee, and G. R. Rout, “The soil-borne fungal pathogen Athelia rolfsii: past, present, and future concern in legumes,” *Folia Microbiologica*, no. 0123456789, 2023, doi: 10.1007/s12223-023-01086-4.